

To: Yamada, Richard (Yujiro)[yamada.richard@epa.gov]
From: Bahadori, Tina
Sent: Mon 8/14/2017 3:35:22 PM
Subject: RE: Revised SAB Charge Questions - SAB CAAC Member Preliminary Responses - Literature Search - ETBE and tBA next week

Except for 1:30 -2, I can walk out of any of my meetings to take a call from you. So, just call when you can.

Tina

From: Yamada, Richard (Yujiro)
Sent: Monday, August 14, 2017 11:33 AM
To: Bahadori, Tina <Bahadori.Tina@epa.gov>
Subject: Re: Revised SAB Charge Questions - SAB CAAC Member Preliminary Responses - Literature Search - ETBE and tBA next week

Hi Tina - perhaps I can talk to you all before I talk to him? Are u free later today? Thanks much,
Richard

Sent from my iPhone

On Aug 14, 2017, at 11:26 AM, Bahadori, Tina <Bahadori.Tina@epa.gov> wrote:

Thanks Richard – it is unclear what Kevin wants. These preliminary responses from peer reviewers just set the stage for their discussion during their 3-day meeting this week. These help to figure out where the ‘problem’ areas are for the committee to spend time on. Having met Kevin on Friday (during the meeting with OMB), I have interesting insights both into his thinking and his motivations – will be glad to fill you in when you have a moment to breathe and catch up! I would like to fill you in on that OMB meeting anyway.

Tina

From: Yamada, Richard (Yujiro)
Sent: Monday, August 14, 2017 11:14 AM
To: Bahadori, Tina <Bahadori.Tina@epa.gov>
Subject: Fwd: Revised SAB Charge Questions - SAB CAAC Member Preliminary Responses - Literature Search - ETBE and tBA next week

FYI - I will call him sometime soon - I believe he called me late Friday - thanks

Sent from my iPhone

Begin forwarded message:

From: "Beck, Nancy" <Beck.Nancy@epa.gov>
Date: August 11, 2017 at 5:36:23 PM EDT
To: "kevin.bromberg@sba.gov" <kevin.bromberg@sba.gov>
Cc: "Zarba, Christopher" <Zarba.Christopher@epa.gov>, "James_H_Kim@omb.eop.gov" <James_H_Kim@omb.eop.gov>, "Yamada, Richard (Yujiro)" <yamada.richard@epa.gov>
Subject: Re: Revised SAB Charge Questions - SAB CAAC Member Preliminary Responses - Literature Search - ETBE and tBA next week

Hi Kevin,

You may want to discuss SBA concerns with Richard Yamada who is the DAA in ORD.

I've cc'd him here.

Regards

Nancy.

Nancy B. Beck, Ph.D., DABT
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On Aug 11, 2017, at 2:22 PM, Bromberg, Kevin L. <kevin.bromberg@sba.gov> wrote:

The EPA IRIS program presents the standard softball literature search question used in previous reviews, but which has been noticeably improved in at least two recent IRIS reviews:

Current Question #1:

Please comment on the strategies for literature searches, criteria for study inclusion or exclusion and evaluations of study methods and quality discussed in the Literature Search Strategy/Study Selection and Evaluation section. Were the strategies clearly described and objectively applied?

Here is a more robust literature search question based on the question from BaP and ammonia reviews employed by the SAB (2014?) after modifying the question above:

Proposed Revised Question #1:

The process for identifying and selecting pertinent studies for consideration in developing the assessment is detailed in the *Literature Search Strategy/Study Selection and Evaluation* section. Please comment on whether the literature search approach, screening, evaluation, and selection

of studies for inclusion in the assessment are clearly described and supported. **Please comment on whether EPA has clearly identified the criteria (e.g., study quality, risk of bias) used for selection of studies to review, the influential studies to select for inclusion in the assessment, and the key studies used in the development of reference values. Can you recommend improved approaches or criteria to be employed by the agency?** Please identify any additional peer-reviewed studies from the primary literature that should be considered in the assessment of noncancer and cancer health effects of tBA and ETBE.

This revised question addresses – should EPA have chosen a different approach, or how can the approach be improved? This question addresses whether EPA selected the correct criteria for screening, evaluation and selection. This question specifically asks about the selection of studies for the development of reference values. This question asks about the omission of additional peer-reviewed studies, although later charge questions may remedy this omission in part. Using a robust question is an opportunity to improve the assessment taken by the BaP and Ammonia panels not taken by this panel. EPA has the opportunity to perform an improved literature search/study collection based on peer review advice.

The identification of the appropriate literature and identification of the key studies for development of reference values, for example, is extremely important, and yet the EPA question did not yield significant substantive advice on these issues. See responses below.

An asterisk * denotes – assigned to Literature Charge Question

Dr. Deborah A. Cory-Slechta*

1. Literature Search Strategy/ Study Selection and Evaluation-Systematic Review Methods. Please comment on the strategies for literature searches, criteria for study inclusion or exclusion and evaluations of study methods and quality discussed in the Literature Search Strategy/Study Selection and Evaluation section. Were the strategies clearly described and objectively applied?

The literature search and study selection were clearly described and objectively applied. In addition, the criteria for inclusion are well described and appropriate inclusion and exclusion criteria, as well as criteria of study quality for inclusion applied.

Dr. W.M. Foster*

1. Literature Search Strategy/Study Selection and Evaluation.

I found the keywords selected for search using the online venues of scientific databases (PubMed, Toxline, Web of Science, and TSCATS) to be appropriate for ETBE. The resulting Table information defining the searched literature, Tables LS-1, LS-2 (review reports), and LS-3, were lucid and identified the temporal end point (Nov, 2015) of the applied searches, and the inclusion/exclusion criteria utilized. The overall success of the search approach as presented in Fig. LS-1 seemed adequate. The search selections appeared appropriate and on target for determining health effects of exposure to ETBE in animal models for extension to humans.

Dr. Karen Chou

1. Literature Search Strategy/Study Selection and Evaluation.

Yes, the strategies are clearly described.

Recommended correction, p. 1-2, Line 7: Citation mistake. It should be Nihlen et al., "1998a".

Dr. Harvey Clewell

1. Literature Search Strategy/ Study Selection and Evaluation

I found the strategies for literature searching, study inclusion and evaluation to be clearly described and objectively applied.

Dr. Deborah A. Cory-Slechta*

1. Literature Search Strategy/ Study Selection and Evaluation

Yes, the strategies were clearly described and objectively applied. An extensive search was undertaken after which inclusion and exclusion criteria were applied and these criteria were appropriate, including elimination of studies of mixtures exposures as the toxicological review is specific to tert-butyl alcohol and thus mixture studies introduce problems of defining sources of the mixture responsible for an effect. In addition, the criteria used for evaluation were also appropriate with respect to suitability for inclusion in derivation of reference doses/concentrations.

Dr. W.M. Foster*

1. Literature Search Strategy/Study Selection and Evaluation.

I found the keywords selected for search using the online venues of scientific databases (PubMed, Toxline, Web of Science, and TSCATS) to be appropriate for tBA. The resulting Table information defining the searched literature: Tables LS-1, LS-2 (review reports) were lucid and identified the temporal end point (May, 2015) of the applied searches, and Table LS-3 clearly listed the inclusion/exclusion criteria utilized for valuation of reports downloaded from the literature searches. Success of the search approach as overviewed in Fig. LS-1 seems adequate. One concern at this point, is the reliance on older reports, for example, the animal model data base (n=14 reports in total, pg. LS-8) utilized for validity of injury and assessing risk, all were accomplished prior to 1998, except for a single, industry sponsored, reproductive study accomplished in 2004.

The summarization of animal model studies utilized and listed in Table 1-5 (pg. LS-8), provide, and establish an understanding of the reproducibility of the animal model data base for modes of exposure (oral, inhalation), duration of exposure (sub-chronic, chronic), and scope or focus (developmental, neurodevelopmental, reproductive) of the subsequent to exposure, tBA-induced injury. The search selections appear appropriate and on target for determining health effects of oral exposure to tBA in animal models for extension to humans.

A report that appeared later in time (online, 2016) than the May, 2015, cut-off date for search inventory, given its subject matter would be reasonable to review for information pertinent to pharmacokinetic models of tBA using oral exposure; additionally, the report

supports a male-rat-specific mode of action for tBA-induced kidney tumors [SJ Borghoff et al, J. Appl. Toxicol. 37: 621–640 (2017)].

Dr. Karen Chou

1. Literature Search Strategy/ Study Selection and Evaluation- Systematic Review Methods.

Yes, the strategies are clearly stated.

Dr. Harvey Clewell

1. Literature Search Strategy/ Study Selection and Evaluation- Systematic Review Methods.

I found the strategies for literature searching, study inclusion and evaluation to be clearly described and objectively applied.

Hazard Identification and Dose-Response Analysis.

Chapter 1 (Hazard Identification) and the supplemental materials summarize the chemical properties, toxicokinetics, and health effects associated exposure to tert-butanol. Chapter 2 (Dose Response Analysis) uses this information to derive an oral reference dose and inhalation reference concentration for noncancer outcomes, in addition to an oral slope factor for cancer.

Dr. James Bruckner Preliminary Comments 8/9/17 *

Ethyl Tertiary Butyl Ether (ETBE) Charge Questions

1. Literature Search Strategy/Study Selection and Evaluation Systematic Review Methods

The scientific literature search and screening strategy were clearly described on pp. xxvii – xxxiv of the IRIS document. This was a very thorough and effective approach to identify the most pertinent publications. Tables summarizing what appears to be the more important health effects information were constructed as recommended by the NRC (2011). This allows readers to survey and compare results/data available on particular health effects and species. I found the detailed evaluations of the 30 key study design and quality considerations useful.

These are not surprising responses from this question posed by the IRIS program which focuses on “clear” descriptions “objectively” applied.